FORM PTO-1390 (REV. 9-2001) U S DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY'S DOCKET NUMBER	U S APPLICATION NO (If known, see 37 CFR 1 5)
2354/140	10/009139

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/AU00/00107	16 February 2000 (16.02.00)	

TITLE OF INVENTION
ANTIMICROBIAL POLYMERIC COMPOSITIONS

APPLICANT(S) FOR DO/EO/US MELROSE, Graham John Hamilton; DALY, Gerry and HUXHAM, Andrew James

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. [X] This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. [ ] This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. [X] This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (21) indicated below.
4. [X] The US has been elected by the expiration of 19 months from the priority date (Article 31).
5. [X] A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   a. [ ] is attached hereto (required only if not communicated by the International Bureau).
   b. [X] has been communicated by the International Bureau.
   c. [ ] is not required, as the application was filed in the United States Receiving Office (RO/US).
6. [ ] An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)).
   a. [ ] is attached hereto.
   b. [ ] has been previously submitted under 35 U.S.C. 154(d)(4).
7. [ ] Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
   a. [ ] are attached hereto (required only if not communicated by the International Bureau).
   b. [ ] have been communicated by the International Bureau.
   c. [ ] have not been made; however, the time limit for making such amendments has NOT expired.
   d. [ ] have not been made and will not be made.
8. [ ] An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371 (c)(3)).
9. [X] An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).
10. [ ] An English language translation of the annexes of the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11 to 20 below concern document(s) or information included:

11. [X] An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. [X] An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. [X] A FIRST preliminary amendment.
14. [ ] A SECOND or SUBSEQUENT preliminary amendment.
15. [ ] A substitute specification.
16. [ ] A change of power of attorney and/or address letter.
17. [ ] A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 35 U.S.C. 1.821 - 1.825.
18. [ ] A second copy of the published international application under 35 U.S.C. 154(d)(4).
19. [ ] A second copy of the English language translation of the international application under 35 U.S.C. 154(d)(4).
20. [X] Other items or information:

Applicants claim Small Entity status.
A copy of the Preliminary Examination Report with amended pages.

U S APPLICATION NO (if known, see 37 CFR 1.5)	INTERNATIONAL APPLICATION NO	ATTORNEY'S DOCKET NUMBER
10/009139	PCT/AU00/00107	2354/140

21. [X] The following fees are submitted:	CALCULATIONS PTO USE ONLY
BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)):	
Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO **$1040.00**	
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO **$890.00**	
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO **$740.00**	
International preliminary examination fee (37 CFR 1.482) paid to USPTO but all claims did not satisfy provisions of PCT Article 33(1)-(4) **$710.00**	
International preliminary examination fee (37 CFR 1.482) paid to USPTO and all claims satisfied provisions of PCT Article 33(1)-(4) **$100.00**	
ENTER APPROPRIATE BASIC FEE AMOUNT =	$ 1,0400.00
Surcharge of **$130.00** for furnishing the oath or declaration later than [ ] 20 [ ] 30 months from the earliest claimed priority date (37 CFR 1.492(e)).	$ 0.00

CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE	
Total claims	19 - 20 =	0	x **$18.00**	$ 0.00
Independent claims	1 - 3 =	0	x **$84.00**	$ 0.00
MULTIPLE DEPENDENT CLAIM(S) (if applicable)			+ **$280.00**	$ 0.00

TOTAL OF ABOVE CALCULATIONS =	$ 1,000.00
[X] Applicant claims small entity status. See 37 CFR 1.27. The fees indicated above are reduced by 1/2. +	$ 500.00
SUBTOTAL =	$ 500.00
Processing fee of **$130.00** for furnishing the English translation later than [ ] 20 [ ] 30 months from the earliest claimed priority date (37 CFR 1.492(f)).	$ 0.00
TOTAL NATIONAL FEE =	$ 500.00
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). **$40.00** per property +	$ 40.00
TOTAL FEES ENCLOSED =	$ 540.00
Amount to be refunded:	$
charged:	$

a. [X] A check in the amount of $ 540.00 to cover the above fees is enclosed.

b. [ ] Please charge my Deposit Account No. _____ in the amount of $ _____ to cover the above fees. A duplicate copy of this sheet is enclosed.

c. [X] The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 14-1138 . A duplicate copy of this sheet is enclosed.

d. [ ] Fees are to be charged to a credit card. **WARNING:** Information on this form may become public. **Credit card information should not be included on this form.** Provide credit card information and authorization on PTO-2038.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137 (a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO.

Joseph M. Noto
Nixon Peabody LLP
Clinton Square
P. O. Box 31051
Rochester, NY 14603-1051
United States of America

Joseph M. Noto
SIGNATURE

Joseph M. Noto
NAME

32,163
REGISTRATION NUMBER

Docket No: **2354/140**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: **Graham John Hamilton, Melrose, Gerry Daly, & Andrew James Huxham**

U.S. Serial No.: **To be assigned**

Filed: **Herewith**

PCT International Application No.: **PCT/AU00/00107**

Filed: **16 February 2000**

For: **ANTIMICROBIAL POLYMERIC COMPOSITIONS**

PRELIMINARY AMENDMENT

Commissioner of Patents
and Trademarks
Washington, D.C. 20231
BOX: PCT

Dear Sir:

Please amend the above-identified patent application as follows:

In the Claims:

7. A method according to claim 2 wherein the solvent includes an alkali selected from an alkali hydroxide, alkali carbonate and mixtures thereof.

8. A method according to claim 2 wherein the alkali is sodium hydroxide, sodium carbonate or mixture thereof.

12. A method according to claim 1, characterised in that the solution is heated for a period of between 1 to 1,400 hours, thereby increasing antimicrobial activity of the polymers.

13. A method according to claim 1, characterised in that the solution is heated for a period in the range of from 4 to 60 hours.

16. A method according to claim 1, characterized by the addition of base or alkali to the polymers before and/or during heating, thereby enhancing the antimicrobial activity of the polymers.

17. A method according to claim 1, characterised in that the release of free acrolein monomer by the acrolein polymer is reduced.

18. An antimicrobial compound or composition prepared by the method of claim 1.

19. A preservation disinfectant or antiseptic or composition prepared wholly or in part by method of claim 1.

REMARKS

Entry of the foregoing prior to the initial office action on the merits is respectfully requested. Pursuant to 37 C.F.R. § 1.121, attached as Appendix A is a version with markings to show changes made to the claims.

Early allowance of the pending claims is hereby earnestly solicited.

Respectfully submitted,

Date: Nov. 8, 2001

Joseph M. Noto
Registration No. 32,163

Nixon Peabody LLP
Clinton Square, P. O. Box 31051
Rochester, New York 14603
Telephone: 716/263-1601
Facsimile: 716/263-1600

APPENDIX A

Version With Markings to Show Changes Made

In reference to the amendments made herein to claims 7, 8, 12, 13, 16, 17, 18, and 19, additions appear as underlined text, while deletions appear as bracketed text, as indicated below:

In The Claims:

7. A method according to claim 2 [or claim 3] wherein the solvent includes an alkali selected from an alkali hydroxide, alkali carbonate and mixtures thereof.

8. A method according to claim 2 [or claim 3] wherein the alkali is sodium hydroxide, sodium carbonate or mixture thereof.

12. A method according to [any one of claims 1 to 3] claim 1, characterised in that the solution is heated for a period of between 1 to 1,400 hours, thereby increasing antimicrobial activity of the polymers.

13. A method according to [any one of the preceding claims] claim 1, characterised in that the solution is heated for a period in the range of from 4 to 60 hours.

16. A method according to [any one of the preceding claims] claim 1, characterized by the addition of base or alkali to the polymers before and/or during heating, thereby enhancing the antimicrobial activity of the polymers.

17. A method according to [any one of the preceding claims] claim 1, characterised in that the release of free acrolein monomer by the acrolein polymer is reduced.

18. An antimicrobial compound or composition prepared by the method of [any one of the preceding claims] claim 1.

19. A preservation disinfectant or antiseptic or composition prepared wholly or in part by method of [any one of claims 1 to 16] claim 1.

TITLE

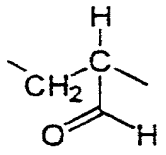
"ANTIMICROBIAL POLYMERIC COMPOSITIONS"

FIELD OF THE INVENTION

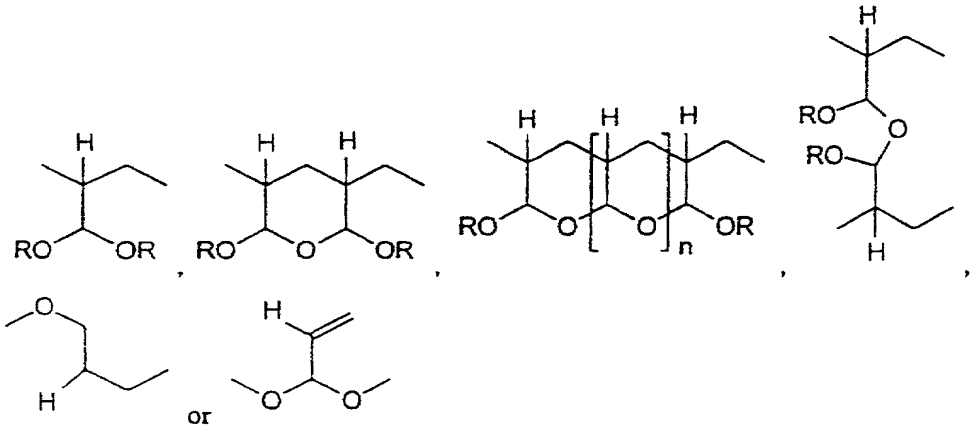
The present invention relates to antimicrobial polymeric compositions. More particularly, the antimicrobial polymeric compositions of the present invention contain compounds having a polyacrolein sub-unit with its aldehyde group in its free, hydrated, hemi-acetal or acetal form, and having biostatic and/or biocidal properties. The invention is directed to compositions containing these polymeric compounds and the biostatic and/or biocidal uses of these compositions.

BACKGROUND ART

The broad-based antimicrobial properties of polymers (hereinafter called the "subject polymers") having the repeating polymeric unit:



; or this unit in its hydrated, hemi-acetal or acetal form, represented by the formulae:



wherein R is hydrogen or alkyl and n is an integer of one or more, have been demonstrated previously (Melrose et al., International Patent Publication WO 88/04671). The subject polymers described therein include poly(2-propenal, 2-propenoic acid).

It has also been noted previously (Melrose, International Patent Publication WO 96/38186) that poly(2-propenal, 2-propenoic acid) is formed when the aldehyde groups of poly(2-propenal) *syn* polyacrolein are partially auto-oxidised to carboxyl groups, by heating the dry polymer in air, to 100°C and preferably to between 80°C and 100°C. It was further noted that the resulting polymer is soluble in dilute aqueous bases, for example aqueous sodium carbonate.

An earlier disclosure (Werle et al., Australian Patent Application 11686/95, now lapsed) claimed solubility of the subject polymers in polyols – but not solubility in aqueous media, following heating to 75°C. It was further claimed that subsequent to the heating to 75°C, brief treatment with sodium hydroxide gave rise to aqueous solubility and apparently as a result, increased antimicrobial activity.

To increase the stability of compositions containing the subject polymers, Melrose & Huxham (International Patent Application PCT/AU99/00578) have formulated compositions with anionic surfactants. Additionally, this prior art revealed that in basic compositions, in contrast to acidic compositions, the subject polymers have faster antimicrobial activity, but are less stable.

It is particularly desirable that the subject polymers should not be unstable, yielding acrolein, as this monomer is very irritating to the eyes, lungs, tissues and skin.

It is one object of the present invention to provide methods of preparing compositions, these methods producing a new configuration of the subject polymers and in particular of poly(2-propenal, 2-propenoic acid), and which have enhanced antimicrobial activity.

It is a further object of the present invention to provide methods of preparing compositions, these methods producing a new configuration of the subject polymers and in particular of poly(2-propenal, 2-propenoic acid), and which better retain antimicrobial activity.

It is a still further object of the present invention to provide methods of preparing compositions, these methods producing a new configuration of the subject polymers and in particular of poly(2-propenal, 2-propenoic acid), and which contain less free acrolein.

It is a yet still further object of the present invention to provide compositions containing a new configuration of the subject polymers and in particular of poly(2-propenal, 2-propenoic acid) which are efficacious disinfectants or antiseptics.

Throughout the specification, unless the context requires otherwise, the word "comprise" or variations such as "comprises" or "comprising", will be understood to imply the inclusion of a stated integer or group of integers but not the exclusion of any other integer or group of integers.

DISCLOSURE OF THE INVENTION

In accordance with the present invention there is provided a method for improving the antimicrobial activity of a polymer derived from acrolein monomer wherein the polymer has been oxidized in air to form an oxidised acrolein polymer comprising carboxyl groups, said method comprising:

providing a solution of the oxidized acrolein polymer comprising carboxyl groups in a mixture containing water and a hydroxylic solvent including an alcohol selected from the group consisting of polyols, polyethylene glycols and alkanols; and

heating the solution at a temperature in the range of from 40 to 150^{o}C for a period sufficient to improve the antimicrobial activity of the acrolein polymer.

Still preferably, the polymers are heated in the range of 40 to 115°C.

Still further preferably, the polymers are heated in the range of 70 – 90°C.

Preferably, the polymers are heated for a period of between 1 to 1,400 hours, thereby increasing antimicrobial activity of the polymers.

Still preferably, the polymers are heated for a period of between 10 to 60 hours.

In one form of the invention the polymers are heated in the presence of one or more of polyethylene glycol, polyol or alkanol, thereby providing one or both of enhanced stability or enhanced antimicrobial activity. Water is invariably present in these alcohols.

Preferably, polyethylene glycol is present during the preparation of the polymers in the amount of between 50 and 99% by weight.

Still preferably, polyethylene glycol is present during preparation of the polymers in the amount of between 64 and 95% by weight.

In a further form of the invention, base or alkali is added to the polymers before and/or during heating, thereby enhancing the antimicrobial activity of the polymers.

Preferably. the addition of the base or alkali brings the pH of the polymers to between 7 and 9.

Still preferably, the pH is about 8. Sodium hydroxide may be the base added.

In a still further form of the invention, the release of free acrolein monomer is inhibited, thereby the polymers are less likely to present a source of tissue or dermal irritation.

Preferably, the polymer is initially heated, predominantly in the dry state, to between 80 and 100°C.

Still preferably, the polymer is initially heated to about 85°C.

In accordance with the present invention there is further provided an antimicrobial compound or composition prepared by one or more of the methods described hereinabove.

In accordance with the present invention there is still further provided a preservative compound or composition prepared by one or more of the methods described hereinabove.

In accordance with the present invention there is yet still further provided a disinfectant or antiseptic compound or composition prepared wholly or in part by the methods described hereinabove.

Preferably, the disinfectant or antiseptic compound or composition has a pH greater than 6, thereby enhancing antimicrobial activity.

In accordance with the present invention, there are provided methods for the preparation of a new configuration of the subject polymers including poly(2-propenal, 2-propenoic acid) and of compositions therefrom, whereby the compositions exhibit increased antimicrobial activity, and/or increased stability and/or contain less free acrolein, thus making the polymers and/or their compositions more suitable as preservatives, and/or active ingredients in disinfectants and/or, antiseptics, under acidic or basic conditions.

BEST MODE(S) FOR CARRYING OUT THE INVENTION

Since the prior art recorded some instability of poly(2-propenal, 2-propenoic acid), as evidenced by loss of antimicrobial activity of its compositions, the routine procedure in industry was then followed in our laboratories, of quantitatively determining this instability by standard "accelerated ageing" at elevated temperature, ie. at 40°C. However, to our greatest surprise, the elevated temperature of "ageing" poly(2-propenal, 2-propenoic acid) in aqueous or in aqueous-polyethylene glycol solutions at 40°C, not only slowed the decrease in antimicrobial activity – but in fact, actually increased antimicrobial activity of the

poly(2-propenal, 2-propenoic acid), see Example 2(a) and (b). This finding is totally contradictory and unexpected in view of the prior art which predicts that the rise in temperature should lead to "accelerated ageing", ie. accelerated loss of antimicrobial activity.

Henceforth, the process of providing increased antimicrobiological activity by the formation of a new configuration of the subject polymers including poly(2-propenal, 2-propenoic acid), is referred to as "super-activation" and the polymers referred to as "super-activated polymers".

Even more surprising, in view of prior art, the inventors have found super-activation in aqueous polyethylene glycol solution is promoted by basic conditions, see Example 2(c).

Also, super-activation is promoted by heat and moisture, alone, see Example 4.

Additionally, it has been found that prior, dry heating of the subject polymers between 80–85°C gives polymers, see Example 1, which are soluble in aqueous media and suitable for subsequent super-activation.

Super-activation is facilitated by the presence of polyethylene glycols or polyols or alkanols see Example 3, – we believe, since the presence of the polyethylene glycol or polyol or alkanol protects and stabilises the carbonyl groups of the polymers, possibly by formation of acetals, from alkaline degradation by the Cannizarro reaction.

An added advantage of super-activation is that it gives rise to less, contaminant acrolein which is a source of tissue and dermal irritation, see Example 6.

It is emphasised that super-activation is quite distinct and additional to any increase of antimicrobial activity which may result, merely from more polymer being available in any aqueous test-medium as the result of increased

hydrophillicity of the polymer such as was demonstrated in lapsed Australian Patent Application AU-A-11686/95 (hereinafter "11686/95"). The inventors have repeated exactly the method described in 11686/95 and then, following, found that subsequent super-activation of the partially soluble polymer demonstratively gave rise to additional, substantial antimicrobial activity, see Example 5. It should be noted that even super-activation did not render the polymer from 11686/95 completely soluble – in contrast to super-activation beginning with polymer firstly heated between to 80 – 85°C.

The optimum time to achieve super-activation of solutions of poly(2-propenal, 2-propenoic acid) depends inversely upon the temperature, see Example 7. It will be apparent that even ageing at room temperature may be used for super-activation, especially when facilitated in the presence of hydroxylic solvent and/or base, but obviously, this may be impractical due to the longer time periods required.

The inventors have found polymers super-activated as described herein, suitable for preservatives in water-based products or processes, and as well, as active ingredients in disinfectants or antiseptics having the advantage of enhanced antimicrobial activity, see Example 8. Furthermore, the inventors found that the antimicrobial activity of such disinfectants or antiseptics was increased by increase in their pH, for example above pH 6, see again Example 8.

The invention will now be described with reference to several Examples, which should not be construed as limiting the scope thereof.

BIOCIDAL TEST

Dilute sample with 1% aqueous sodium bicarbonate to obtain the required concentration (unless specified to the contrary, 0.125% in polymer). Weight 19.9g of diluted sample into a sterile jar and inoculate with 0.1 mL of 10^7 – 10^8 suspension of *Ps.aeruginosa* and mix. At specified time-intervals, transfer 1 mL of

inoculated sample to 9 mL of letheen broth and vortex. Plate out serial 1 in 10 dilutions. Pour with tryptone soya agar. Incubate 3 days at 37°C.

EXAMPLE 1

The example describes a method of preparing a poly(2-propenal, 2-propenoic acid) by oxidation of a solid acrolein polymer in air. This poly(2-propenal, 2-propanoic acid) is the preferred method of preparing a starting material for use in the method of the invention. Water (720 mL at ambient temperature, about 20°C) and acrolein (60g; freshly distilled, plus hydroquinone added to 0.25% w/w) were placed in an open beaker, within a fume cupboard, and very vigorously stirred, mechanically. Then, 0.2 M aqueous sodium hydroxide (21.4 mL) was added to bring the pH to 10.5 – 11.0. The solution immediately turned a yellow typical of the hydroquinone anion and within a minute, the colour had disappeared and the clear solution became milky. About 1 minute later, precipitation of a white crystalline, flocculent polymer began, and appeared complete within 15-30 minutes. The precipitate was filtered and washed with water (250 mL), dried at room temperature upon filter papers for 2 days (yield 25g), then spread as a thin layer in glass petri dishes and heated at 40°C/8 hours. This heating was continued at the following schedules : 50°C/15 hours; 65°C/4 hours; 75°C/18 hours; 84°C/24 hours.

It is envisaged that this method may be scaled-up to include, eg the stepwise addition of acrolein, in a closed vessel, and followed by more rapid drying.

Typically, a solution of the resulting poly(2-propenal, 2-propenoic acid) was prepared by adding 2g of the subject polymer, with stirring over 15-30 minutes, to a 1% w/w aqueous sodium carbonate solution (100 mL), and then diluted as required. Such solutions were perfectly clear – in contrast to attempted dissolutions, using alternatively, polymer derived from Example 5 of 11686/95; compare Example 5, hereinafter.

EXAMPLE 2

(a) 5g of poly(2-propenal, 2-propenoic acid) was dissolved in 64g polyethylene glycol ("PEG") 200 and combined with 31g of a 0.71% solution of sodium carbonate. A portion of the solution (apparent pH=5.8) was retained at room

temperature while the remainder was heated at 60°C for periods of 12 or 25 days. Samples were diluted with 1% sodium bicarbonate and submitted for biocidal testing at polymer concentrations of 0.125% w/w. Surprisingly, the samples which had undergone "accelerated ageing" showed improved antimicrobial activity, as can be seen by reference to Table 1:

Table 1

	Cfu/ml * *(Pseudomonas aeruginosa)*				
Sample, heated	0 min	10 min	15 min	30 min	60 min
25 days at room temperature	7.8×10^6	4.1×10^6	6.1×10^5	9.8×10^4	<10
12 days at 60°C	7.7×10^6	1.4×10^6	9.8×10^3	<10	<10
25 days at 60°C	1.0×10^7	1.3×10^6	6.6×10^4	<10	<10

* Colony forming units/mL

(b) 1g poly(2-propenal, 2-propenoic acid) was dissolved in 200 ml of 0.1% Na_2C0_3 and allowed to stand overnight. Sodium lauryl sulphate was introduced at a level of 0.05% and the solution was acidified with HCl to pH 5.9. Portions were stored at both room temperature and 60°C. Biocidal Tests were carried out on 0.125% polymer solutions, with 1% $NaHCO_3$ used as the diluent. The "aged" sample showed a surprising improvement in performance, as can be seen by reference to Table 2:

Table 2

Sample	Cfu/ml * *(Pseudomonas aeruginosa)*			
	0 min	10 min	15 min	30 min
20 days at room temperature (RT)	9.0×10^6	5.1×10^5	6.8×10^2	<10
7 days at 60°C + 13 days at RT	9.0×10^6	1.2×10^2	<10	<10

* Colony forming units/mL

(c) A 5% solution of super-activated polymer was prepared as in example (2a) but replacing PEG200 with PEG1000. A portion of this solution was treated with conc. NaOH to pH 8.1. Samples were heated at 60°C and submitted for biocidal testing. The sample exposed to more basic conditions unexpectedly gave superior biocidal performance, as can be seen by reference to Table 3:

Table 3

	Cfu/ml * *(Pseudomonas aeruginosa)*				
Sample	0 min	5 min	10 min	15 min	30 min
pH 5.8, 12 days 60°C	3.8×10^6	2.7×10^6	1.5×10^6	3.3×10^3	<10
pH 8.1, 7 days 60°C	9.0×10^6	-	10	<10	<10
pH 8.1, 17 days 60°C	8.3×10^6	3.3×10^5	1.3×10^2	<10	<10

* Colony forming units/mL

EXAMPLE 3

(a) 5% solutions of polymers of a range of degrees of super-activation, apparent pH 5.7, were prepared similarly to Example 2(a), but varying the percentage of PEG 200.

Samples were heated at 60°C and stabilities were monitored over time. Physical stability was considered to have failed with the occurrence of precipitation or gelling. UV measurements were made on a 0.01% polymer concentration in 1% sodium carbonate solution. A decrease of the ratio of absorption at 268 nm : 230 nm is considered synonymous with a decrease in chemical stability. Results are shown in Table 4:

Table 4

Composition	A	B	C	D
PEG 200 (% by weight)	0	50	64	95
Physical Stability				
Time	A	B	C	D
4 days 60°C	Fail	Pass	Pass	Pass
11 days 60°C	Fail	Fail	Pass	Pass
Chemical Stability	Ratio $\frac{260-270 \text{ peak absorbance}}{228-235 \text{ peak absorbance}}$			
Time	A	B	C	D
0 days 60°C	1.38	1.41	1.43	1.46
4 days 60°C	0.98	1.04	1.21	1.27
11 days 60°C	-	0.97	1.03	1.09
18 days 60°C	-	0.89	0.92	1.04
25 days 60°C	-	-	0.84	1.04

Both physical and UV spectral results demonstrate the positive effect of PEG on stability; higher PEG content results in greater physical and chemical stabilities.

(b) The following solutions A and B were prepared by dissolving 4g of poly(2-propenal, 2-propenoic acid) in 196 g 1% sodium bicarbonate and adjusting the pH to 7 (A) and 5.5 (B) with dilute HCl. Solution C was prepared by dissolving 50g of poly(2-propenal, 2-propenoic acid) in PEG 200 (640g) at 65^0 – 70°C. Then a solution of 4g sodium carbonate in water (306g) was added, the apparent pH being 7, and then 5.5 at the end of the treatment period of 31 days.

All samples were stored at 40°C. At various time intervals samples containing equivalent to 0.125% polymer were submitted for biocidal testing. Results are shown in Table 5:

Table 5

Time(days) at 40°C	Time for complete kill (minutes) <10 cfu/ml *Pseudomonas aeruginosa*		
	Solution A	Solution B	Solution C
0	30	30	30
7	30	60	-
14	-	-	10
31	60	60	10

EXAMPLE 4

1g of poly(2-propenal, 2-propenoic acid) was heated in either a dry or a humid, enclosed chamber, both at 60°C, for 3 days. Solutions of the dry polymer and the humidified polymer, respectively were prepared at 0.125% w/v (with correction for moisture content) and submitted for evaluation by the Biocidal Test :

Table 6

	Cfu/ml * *(Pseudomonas aeruginosa)*					
	0 min	5 min	10 min	15 min	30 min	60 min
Polymer (dry)	4.9×10^6	-	7.6×10^5	5.9×10^4	1.2×10^2	<10
Polymer (humidified)	1.1×10^7	6×10^6	3.4×10^3	3.7×10^3	<10	-

* Colony forming units/mL

The polymers exhibited carbonyl and/or carboxyl absorption in the I.R. between 1700 – 1730 cm^{-1}, carbonyl groups (e.g. with Schiff's reagent) and have M_w = *ca.* 10000 and M_n = *ca.*5000; titration shows carboxyl groups *ca.*5 mole %. These parameters are similar (but not the same) as those of poly(2-propenal, 2-propenoic acid).

EXAMPLE 5

In duplicate experiments, a sample of polymer was prepared and then dissolved in ethane diol, exactly as described in Example 5 of 11686/95. Half of this material was further heated at 80°C for 24 hours (following which, solubility in aqueous media remained incomplete). The samples were compared for antimicrobial activity, using the standard Biocidal Test. Both of the samples treated by heating, ie. super-activation showed a clear enhancement of antimicrobial activity, as shown in Table 7:

Table 7

	Cfu/ml * *(Pseudomonas aeruginosa)*				
Treatment of solution	Initial Count	5 min	10 min	15 min	30 min
(1) None	4.6×10^6	5.7×10^5	2.9×10^2	<10	<10
(2) None	4.6×10^6	4.2×10^5	1.5×10^2	10	<10
(1) 24 hours 80°C	4.6×10^6	3.7×10^6	<10	<10	<10
(2) 24 hours 80°C	4.6×10^6	8.0×10^5	<10	<10	<10

* Colony forming units/mL

EXAMPLE 6

50g of poly(2-propenal, 2-propenoic acid) was dissolved in PEG 200 (640g) at 65 - 70°C. Then, an aqueous solution of sodium carbonate (4g) in water (306g) was added. The sample was divided and either stood at room temperature or heated at 80°C for 24 hours. The acrolein content of the solution was determined over time, by reverse phase HPLC and results are shown in Table 8:

Table 8

Days stored at 20°C	Acrolein Content (ppm)	
	Super-Activated	Not Super-Activated
0	274	144
7	-	126
16	34	103
30	13	80

EXAMPLE 7

Solutions of poly(2-propenal, 2-propenoic acid) were prepared as in Example 6 and treated at temperatures of 40, 60, 80, 100 and 115°C for varying time periods. Samples were subjected to the standard Biocidal Test to confirm the increased kill rate and results are shown in Table 9.

Table 9

Super-activation Temperature (°C)	Optimum Time Range (Hours)	Total Kill Time (minutes)
Room Temperature	>1400	<10
40	1400	<10
60	120 –170	<10
80	16 – 24	<10
100	4 – 7	<10
115	1 – 3	<10

The amount of time required for super-activation is seen to be inversely proportional to temperature. All solutions of polymers derived from the super-activation process were completely miscible, in all proportions, with aqueous solvents.

EXAMPLE 8

(a) 540g of poly(2-propenal, 2-propenoic acid) was dissolved in 2304g PEG200 at 65°C, prior to mixing with 43.2g of sodium carbonate in 712g of water. Then, the solution was heated to 100°C for 4 hours, and 36g sodium lauryl sulphate, 7g ECOTERIC T20 (nonionic detergent) and 2g lemon fragrance were added. The formulation, pH6, was diluted 1:30 with hard water and challenged against

Staphylococcus aureus (a gram-positive bacterium, of particular significance regarding infections in hospitals), and *Salmonella choleraesuis* (a gram-negative bacterium, of particular significance regarding infections in food preparation areas), respectively using the Association of Agricultural Chemists Official Methods of Analysis (1995) 991.47, 991.48, (Hard Surface Carrier Test Method). Results are shown in Table 10:

Table 10

Micro-organism	Positive Tubes	
S aureus	2/60	Pass
S.choleraesuis	1/60	Pass

Adjustment of this formulation to higher pH[s], increases the antimicrobial activity, as monitored by the Biocidal Test. Results are shown in Tables 11(a) and 11(b):

Table 11(a)

Activity against *Staphylococcus aureus*

Initial Count, 3×10^6 cfu/ml; polymer 350 ppm.

pH	10 minutes cfu/ml	20 minutes cfu/ml	30 minutes cfu/ml	45 minutes cfu/ml	60 minutes cfu/ml
5.6	2.8×10^5	4.4×10^4	2.3×10^3	20	<10
7.2	2.7×10^3	<10	<10	<10	<10
8.9	3.2×10^3	<10	<10	<10	<10
10.5	1.1×10^2	<10	<10	<10	<10

Table 11(b)

Activity against *Pseudomonas aeruginosa*

Initial Count, 3.7×10^6 cfu/ml; polymer 350 ppm.

pH	10 minutes cfu/ml	20 minutes cfu/ml	30 minutes cfu/ml	45 minutes cfu/ml	60 minutes cfu/ml
5.6	2.9×10^5	8.6×10^4	6.2×10^2	40	<10
7.2	5.8×10^5	9.1×10^4	4.3×10^3	<10	<10
8.9	9.5×10^5	8.2×10^4	4.6×10^2	<10	<10
10.5	4.5×10^2	3.0×10^3	<10	<10	<10

(b) 1200g of poly(2-propenal, 2-propenoic acid) was dissolved in 7680g of PEG200 at 60°C and then 96g Na_2CO_3 in 3024g water was added. The solution was heated at 100°C for 6 hours.

The formulation was added to the basin of an induced draft cooling tower, to a concentration of 300ppm (30ppm polymer) 3 times/week. Dosing was carried out at evening to allow contact times of 8-12 hours before operation recommenced; residual concentration was expected to be halved every 3 – 6 hours of operation. Recirculation water had on average, temperature 27°C, pH 8.5, conductivity 3000 uS. Microbial counts were determined and compared to an adjacent, identical, tower which was dosed with a biodispersant, daily. Results are shown in Table 12:

Table 12

	Cfu/mL *	
Treatment Time (days)	Treated Tower	Control Tower
1	2.4×10^3	1.1×10^7
2	2.0×10^3	1×10^6
3	3.3×10^3	-
4	2.5×10^3	-
14	6.1×10^4	2.6×10^6
15	5.1×10^4	1.1×10^6
16	5.1×10^4	4.9×10^6

* Colony forming units/mL

The data indicate the treatment programme maintained the microbial counts within the guidelines of AS/NZ Standard 3666.3(Int):1998 and below that in the adjacent tower, containing biodispersant (which was found to be unusually inadequate during the demanding conditions of the very hot, summer period of the test).

Modifications and variation such as would be apparent to the skilled addressee are considered to fall within the scope of the present invention.

CLAIMS

1. A method for improving the antimicrobial activity of a polymer derived from acrolein monomer wherein the polymer has been oxidized in air to form an oxidised acrolein polymer comprising carboxyl groups, said method comprising:

providing a solution of the oxidized acrolein polymer comprising carboxyl groups in a mixture containing water and a hydroxylic solvent including an alcohol selected from the group consisting of polyols, polyethylene glycols and alkanols; and

heating the solution at a temperature in the range of from 40 to 150°C for a period sufficient to improve the antimicrobial activity of the acrolein polymer.

2. A method according to claim 1 wherein said oxidised polymer comprising carboxyl groups is formed by a method of heating a solid acrolein polymer in air at an elevated temperature to form carboxyl groups.

3. A method according to claim 2 wherein said acrolein polymer comprising carboxyl groups has been formed by heating in air at a temperature between 80°C and 100°C.

4. A method according to claim 2 wherein the acrolein polymer comprising carboxyl groups has been formed by heating in air at a temperature of about 85°C.

5. A method according to claim 1 wherein the pH of the solvent is in the range of from 7 to 9.

6. A method according to claim 1 wherein the pH of the solvent is about 8.

7. A method according to claim 2 or claim 3 wherein the solvent includes an alkali selected from an alkali hydroxide, alkali carbonate and mixtures thereof.

8. A method according to claim 2 or claim 3 wherein the alkali is sodium hydroxide, sodium carbonate or mixture thereof.

9. A method according to claim 1, characterised in that the solution is heated in the range of 40 to 115°C.

10. A method according to claim 1, characterised in that the solution is heated in the range of 70-115°C.

11. A method according to claim 9 wherein the solution is heated to about 100°C.

12. A method according to any one of claims 1 to 3, characterised in that the solution is heated for a period of between 1 to 1,400 hours, thereby increasing antimicrobial activity of the polymers.

13. A method according to any one of the preceding claims, characterised in that the solution is heated for a period in the range of from 4 to 60 hours.

14. A method according to claim 11, characterized in that the hydroxylic solvent is polyethylene glycol and is present in the solution in an amount of between 50 and 99% by weight of the solution.

15. A method according to claim 14, characterized in that polyethylene glycol is present in the solution in an amount of between 64 and 95% by weight of the solution.

16. A method according to any one of the preceding claims, characterized by the addition of base or alkali to the polymers before and/or during heating, thereby enhancing the antimicrobial activity of the polymers.

17. A method according to any one of the preceding claims, characterised in that the release of free acrolein monomer by the acrolein polymer is reduced.

18. An antimicrobial compound or composition prepared by the method of any one of the preceding claims.

19. A preservative disinfectant or antiseptic or composition prepared wholly or in part by the method of any one of claims 1 to 16.

COMBINED DECLARATION FOR PATENT APPLICATION AND POWER OF ATTORNEY (Includes Reference to PCT International Applications)	ATTORNEY'S DOCKET NUMBER 2354/140

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

ANTIMICROBIAL POLYMERIC COMPOSITIONS

the specification of which (check only one item below):

[ ] is attached hereto.

[ ] was filed as U.S. Patent Application Serial No. _____ on _____ and was amended on _____ (if applicable).

PCT/AU00/00107 16 February 2000

[X] was filed as PCT International Application Number _____ on _____ and was amended under PCT Article 19 on _____ (if applicable).

I hereby state that I have reviewed and understand the contents of the above-identified specifications, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to the patentability of this application in accordance with Title 37, Code of Federal Regulations, § 1.56(a).

I hereby claim foreign priority benefits under Title 35, United States Code, § 119 of any foreign application(s) for patent or inventor's certificate or of any PCT international application(s) designating at least one country other than the United States listed below and have also identified below any foreign application(s) for patent or inventor's certificate or any PCT international application(s) designating at least one country other than the United States of America filed by me on the same subject matter having a filing date before that of the application(s) of which priority is claimed:

PRIOR APPLICATION(S) AND ANY PRIORITY CLAIMS UNDER 35 U.S.C. 119:

COUNTRY (IF PCT, indicate "PCT")	APPLICATION NUMBER	DATE OF FILING (day, month, year)	PRIORITY CLAIMED UNDER 35 USC 119
PCT	PCT/AU00/00107	16 February 2000	[X] YES [ ] NO
			[ ] YES [ ] NO
			[ ] YES [ ] NO
			[ ] YES [ ] NO
			[ ] YES [ ] NO
			[ ] YES [ ] NO
			[ ] YES [ ] NO
			[ ] YES [ ] NO

COMBINED DECLARATION FOR PATENT APPLICATION AND POWER OF ATTORNEY (Continued) (Includes Reference to PCT International Applications)	ATTORNEY'S DOCKET NUMBER 2354/140

I hereby claim the benefit under Title 35, United States Code, § 120 of any United States application(s) or PCT international application(s) designating the United States of America that is/are listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in that/those prior application(s) in the manner provided by the first paragraph of Title 35, United States Code. § 112. I acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations, § 1.56(a) which occurred between the filing date of the prior application(s) and the national or PCT International filing date of this application:

PRIOR U.S. APPLICATIONS OR PCT INTERNATIONAL APPLICATIONS DESIGNATING THE U.S. FOR BENEFIT UNDER 35 U.S.C. 120:

U.S. APPLICATIONS		STATUS (Check One)		
U.S. APPLICATION NUMBER	U.S. FILING DATE	PATENTED	PENDING	ABANDONED
PCT APPLICATIONS DESIGNATING THE U.S.				
PCT APPLICATION NO.	PCT FILING DATE	U.S. SERIAL NUMBERS ASSIGNED (if any)		

POWER OF ATTORNEY: As a named inventor, I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith. **Michael L. Goldman, Registration No. 30,727; Gunnar G. Leinberg, Registration No. 35,584; Edwin V. Merkel, Registration No. 40,087; Georgia Caton, Registration No. 44,597; Grant E. Pollack, Registration No. 34,097**

Send Correspondence to:	Direct telephone calls to:
Michael L. Goldman, Esq. **NIXON PEABODY LLP** **Clinton Square, P.O. Box 1051** **Rochester, New York 14603**	**Michael L. Goldman** **(716) 263-1304**

201	FULL NAME OF INVENTOR	FAMILY NAME 100 MELROSE	FIRST GIVEN NAME GRAHAM	SECOND GIVEN NAME JOHN HAMILTON
	RESIDENCE & CITIZENSHIP	CITY Dalkeith	STATE/FOREIGN COUNTRY Western Australia, Australia AUX	COUNTRY OF CITIZENSHIP AUSTRALIA
	POST OFFICE ADDRESS	P.O. ADDRESS 20 Nardina Crescent	CITY Dalkeith	STATE & ZIP CODE/COUNTRY Western Australia, 6009, Australia
202	FULL NAME OF INVENTOR	FAMILY NAME 200 DALY	FIRST GIVEN NAME GERRY	SECOND GIVEN NAME
	RESIDENCE & CITIZENSHIP	CITY Gooseberry Hill	STATE/FOREIGN COUNTRY Western Australia, Australia AUX	COUNTRY OF CITIZENSHIP AUSTRALIA
	POST OFFICE ADDRESS	P.O. ADDRESS 16 Aboyne Road	CITY Gooseberry Hill	STATE & ZIP CODE/COUNTRY Western Australia, 6076, Australia
203	FULL NAME OF INVENTOR	FAMILY NAME 300 HUXHAM	FIRST GIVEN NAME ANDREW	SECOND GIVEN NAME JAMES
	RESIDENCE & CITIZENSHIP	CITY Balga	STATE/FOREIGN COUNTRY Western Australia, Australia AUX	COUNTRY OF CITIZENSHIP AUSTRALIA
	POST OFFICE ADDRESS	P.O. ADDRESS 30 Stedham Way,	CITY Balga	STATE & ZIP CODE/COUNTRY Western Australia, 6061, Australia

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

SIGNATURE OF INVENTOR 201	SIGNATURE OF INVENTOR 202	SIGNATURE OF INVENTOR 203
DATE 31/7/01	DATE 14/8/01	DATE 6/8/01